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CITATION:

HIRONAKA, KAZUHIKO. Experimental Study on Fluid Replacement in Puppies : With Special Reference to Pulmonary Arterial and Central Venous Pressures. 日本外科宝函 1970, 39(3): 97-103

ISSUE DATE:

1970-07-01

URL:

http://hdl.handle.net/2433/207883

Arch. Jap. Chir. 39 (3), 97~103, July 1970

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Experimental Study on Fluid Replacement in Puppies:

With Special Reference to Pulmonary Arterial and Central Venous Pressures

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Received for publication June 15, 1970

ITRODUCTION

With recent progress in surgery, the number of diseases indicated for operetion has increased. Accordingly, it is an important problem to evaluate the general condion of the patients, especially, to understand the circulatory dynamics. In most extensive surgical operations proper blood volume replacement is imperative. While the radioisotope technique or the dye dilution method has been used for the measurement of circulatory blood volume, both are unsuitable for serial observations in poor risk patients. HUGHES et al.[8] determined the amount of fluid expected to be given postoperatively by right atrial pressure measured through a catheter placed in the right atrium during surgery. Borow[2)3)] showed that central venous or right atrial pressure, in connection with arterial one, was the most useful guide to blood volume replacement. MOSTERT[10] also stated that a sudden change in circulatory dynamics was better assessed by the measurement of central venous pressure rather than the determination of circulatory blood volume by RISA. However, many factors related to central venous pressure should be first of all understood. LANDIS et al[9]. pointed out that there were many important factors, i. e., capillary pressure (vis a tergo), tonus of the venous wall itself and lateral pressure from the surroundings (vis a latere), the amount of blood in the vein (vis a partie interiore), and function of the right heart (vis a fronte). Frequently, some decrease in the circulatory blood volume causes little or no measurable changes in central venous pressure due to compensatory venospasmus. Even if the circulatory blood volume increases, the rise of central venous pressure is only transient because of Starling's mechanism in response to dilatation of the right atrium and of distensibility of the venous wall.

In hypovolemic shock, massive blood transfusion is undoubtedly effective. However, overtransfusion must be avoided because of the occurrence of pulmonary edema. Hayashi[7] in our laboratory studied on changes of pulmonary circulation following

massive saline infusion in puppies (50 to 100 ml/kg) and obtained the following results.

1. Immediately after the administration of 50ml/kg of saline, the central venous pressure rises abruptly to 7 cm H_2O on the average, and then returns rapidly to the preinfusion level. On the other hand, the pulmonary arterial pressure rises simultaneously to 22cm H_2O(2.5 times as high as the central venous pressure) and 10 minutes later decreases to near the baseline.

2. The change of the central venous and the pulmonary arterial pressure following infusion of 50ml/kg of saline is more pronounced in smaller puppies weighing 500 grams than in larger ones weighing 1 to 2 kilograms, and pulmonary edema is encountered more frequentry in the former.

3. In the larger puppies, the infusion of 100ml/kg of saline results in a marked rise of the central venous pressure, causing acute cardiac failure when it exceeds 20cm H_2O.

4. The administration of isoproterenol before saline infusion slightly accelerates the rise of pulmonary arterial pressure, but the premedication of phenoxybenzamine inhibits this complication.

The present study has been carried out to re-examine the foregoing experimental results using colloidal plasma expander and blood instead of saline, a crystaloid solution.

METHOD

Puppies weighing 1 to 2 kilograms were used. After intramuscular injection of succinylcholine chloride (2mg/kg), intratracheal intubation was done to connect with Infant Circle type anesthetic equipment for artificial respiration with pure oxygen. The animals were fixed in a dorsal position and a catheter was inserted into the right atrium from the right external jugular vein for the measurement of central venous pressure and another was placed in the right femoral artery for the measurement of arterial pressure. Plasma expander or blood was infused through a small tube placed in the right femoral vein. Left thoracotomy was performed in the bed of the 4th. rib. A cannula was inserted in the pulmonary trunk to measure pulmonary arterial pressure. The cannula for arterial pressure was connected with a mercury manometer, while central venous and pulmonary arterial pressures were done with water manometers. For infusion, Plasgen (Kyorin), a colloidal fluid, and fresh homologous blood were used. The fluids of 50 mg/kg were given intravenously as a single dose within 2 minutes.

The pressures were measured before infusion, and then every 5 minutes for 30 minutes. At the end of the experiments animals were sacrificed and lungs were examined macro-and microscopically.

Group 1. In 6 puppies, changes in arterial, central venous and pulmonary arterial pressures were measured after the infusion of Plasgen.

Group 2. In 6 puppies, the corresponding pressures were checked after blood transfusion.

Group 3. In 6 puppies, isoproterenol hydrochloride (Protanol-L : NIKKEN) was

intravenously administered at a rate of 4 μg/kg/min. prior to Plasgen infusion.

Group 4. In 7 puppies, phenoxybenzamine hydrochloride (Dibenzline : Smith Kline and French) of 0.3mg/kg was given intravenously followed by Plasgen infusion.

RESULTS

Group 1. As shown in Fig. 1, the peak of central venous pressure following Plasgen infusion showed 10 cm H_2O, followd by a drop to 4 cm H_2O 10 minuets later. In the group infused with saline (Fig. 2), the peak of central venous pressure exhibited a quite transient rise of 7 cm H_2O and then returned toward near the preinfusion level within 5 minutes. The rise of central venous pressurr was slightly more pronounced and the duration of elevation of the pressure was more prolonged. Pulmonary arterial pressure also increased with a peak of 33cm H_2O indicating a marked rise as compared with a peak of 22cm H_2O in the saline group. After 10 minutes, however, it fell almost to the baseline in both groups.

Group 2. As shown in Fig. 3, the central venous pressure following blood transfusion reached its peak of 15.5cm H_2O, staying at a high level of 30 cm H_2O still 10 minutes later and a level of 5 cm H_2O, above the baseline even after 30

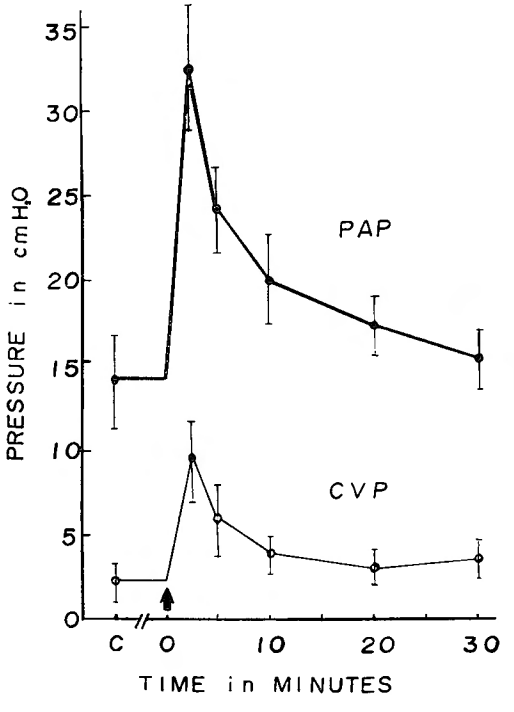

Fig. 1 Changes in pulmonary arterial pressure (PAP) and central venous pressure (CVP) after infusion of Plasgen (50ml/kg).

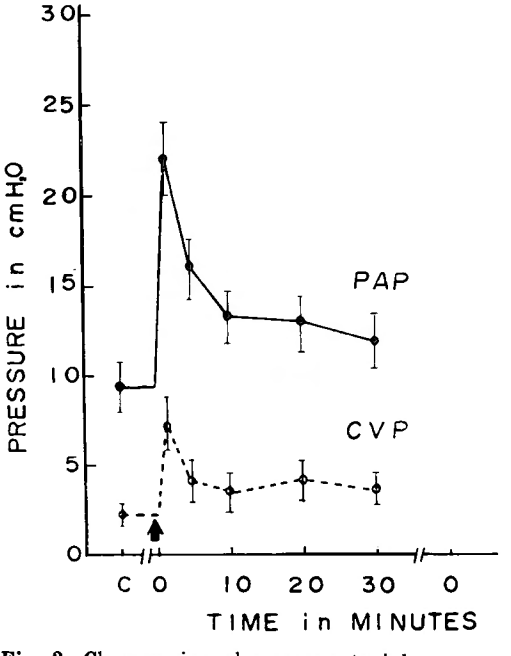

Fig. 2 Changes in pulmonary arterial pressure and central venous pressure after saline infusion (50 ml/kg).

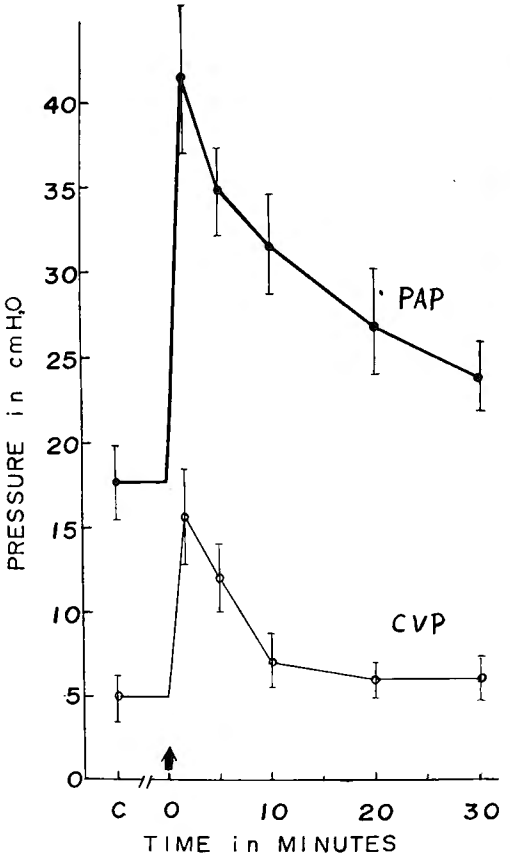

Fig. 3 Changes in pulmonary arterial pressure and central venous pressure after blood transfusion (50 ml/kg).

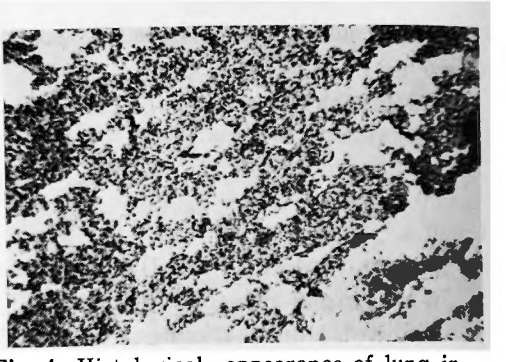

Fig. 4 Histological appearance of lung in Group 2, showing miliary foci of pulmonary edema and congestion.

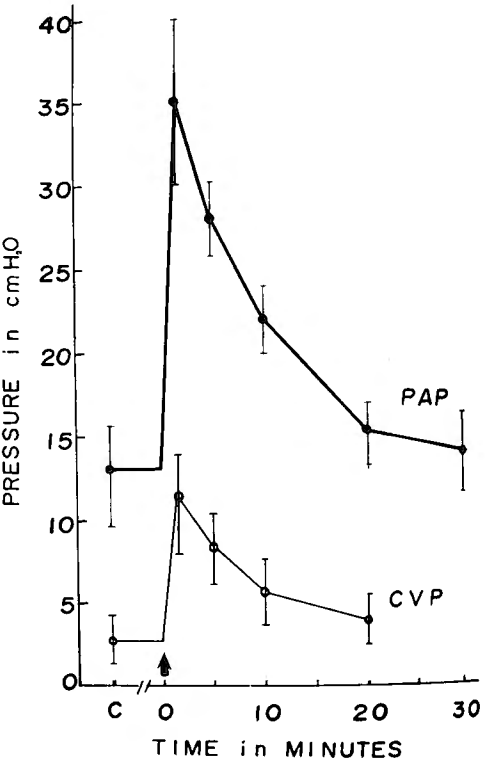

Fig. 5 Changes in pulmonary arterial pressure and central venous pressure after infusion of Plasgen followed by isoproterenol administration.

minutes. At autopsy, miliary foci of pulmonary edema and hemorrhage were noted both macro- and microscopically in 5 of 7 animals (Fig. 4).

Group 3. A peak of 12 cm H_2O of the central venous pressure was noted in this group (a preliminary administration of isoproterenol). The peak of pulmonary arterial pressure (35 cm H_2O) was also higher than in Group 1 (Fig. 5). After 10 minutes, both the central venous pressure and the pulmonary arterial pressure fell relatively rapidly and the later returned to baseline after 20 minutes.

Group 4. In this group (a preliminary administration of phenoxybenzamine) peaks of 9 cm H_2O of the central venous pressure and of 28 cm H_2O of the pulmonary arterial pressure were noted as shown in Fig. 6. These were lower than those in Group 1. The pressure levels after 10 minutes were almost the same in Group 1.

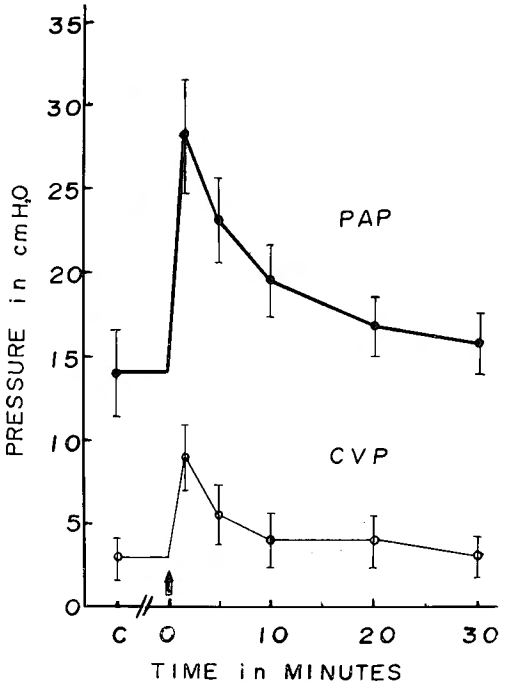

Fig. 6 Changes in pulmonary arterial pressure and central venous pressure after infusion of Plasgen followed by phenoxbenzamine administration.

DISCUSSION

SPENCER et al[13]. noted that increase in the pulmonary arterial pressure was the most reliable sign showing overtransfusion. THOMAS[14] also preferred the right ventricular systolic pressure rather than the central venous pressure as monitor for overtransfusion. In the present study the pulmonary arterial pressure rose beyond 40 cm H_2O upon overtransfusion and fell gradually that it 30 minutes later stayed still above the baseline (Group 3). Histological examination revealed miliary foci of pulmonary edema and hemorrhage in 70% of the puppies. While the central venous pressure showed a peak of 15cm. H_2O immediately, followed by returni ng to near the preinfusion level 10 minutes later. Consequently, the measurement of the central venous pressure along is apparently insufficient to learn whether or not there is overload upon the pulmonary circulatory system.

As stated before, many factors influence the central venous pressure, restoring a normal level during a short time even after a sudden change of the circulatory blood volume. Since the pulmonary circulatory system belong to the low pressure one in which dilatation of the vessel wall and increase of the effective capillary beds take place in response to the increase of pulmonary blood flow, the pressor effect is not so pronounced as in the systemic circulatory system. In a rapid overtransfusion, however, pulmonary hypertension may develop due to the resistence of the capillary bed against a sudden increase in blood flow or to the subsequent exudation in the alveoli leading to miliary pulmonary atelectasis. Pulmonary hypertension became more and more markedly after the infusion of saline, Plasgen and blood in order. Because of the property of Plasgen as a plasma expander, it is thought that this agent leakes out minimal from the blood vessel and stays for a considerable long time within the blood vessel. The present study, however, revealed that pulmonary

hypertension caused by Plasgen infusion returned almost to the preinfusion level after 10 minutes as by saline infusion.

In pulmonary hypertension caused by a sudden increase in pulmonary blood flow the use of isoproterenol at first accelerated this complication because of its inotropic action, and then facilitated falling of both pulmonary arterial and central venous pressures by its vasodilating action. On the other hand, phenoxybenzamine inhibited the occurrence of pulmonary hypertension following massive infusion by its intense dilating action upon the pulmonary artery. As was stated by GREGA et al[6]., the combimed use of isoproterenol and blood transfusion is thought to be the most adequate measures for hypovolemic shock. Phenoxybenzamine appears very effective to prevent pulmonary edema caused by massive infusion.

SUMMARY

In puppies weighing 1 to 2 kilograms, 50ml/kg of colloidal solution (Plasgen) and fresh homologous blood was rapidly intravenously administered. The following results were obtained.

1. The pulmonary arterial pressure rose more than threefold as much as the central venous pressure did after administration of Plasgen and blood.
2. Pulmonary hypertension following massive infusion became more and more pronounced saline, Plasgen and blood in order.
3. Administration of isoproterenol caused a moderate rise of pulmonary arterial and central venous pressures.
4. Use of phenoxybenzamine inhibited the rise of pulmonary arterial pressure following massive infusion of colloidal solution as well as saline.

The gist of this paper was presented at the 7th. General Meeting of The Japanese Sosiety of Pediatric Surgery, Sendai, May 10, 1970.

ACKNOWLEDGMENT

The author is indebted to prof. R. Yamaki for his guidance. The author also is grateful to Assistant Prof. S. Ogino for his kind advise throughout this study.

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和 文 抄 録

仔犬を用いての大量輸液の実験的研究，特に中心静脈圧と肺動脈圧の変動について

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弘 中 和 彦

手術の前後に於ける循環動態の把握は重要であるが循環血液量の変動を連続的に測定できる方法はない．そこで中心静脈圧が用いられるが，これには種々な因子が影響する．

著者は大量輸液(50ml/kg)後の中心静脈圧，肺動脈圧および動脈圧の変動を観察し次の成績を得た．

実験には体重 1～2kg の仔犬を用いた．中心静脈，肺動脈および大動脈内に Tube を挿入し，前2者は水柱マノメーターで，後者は水銀マノメーターで圧を測定した．輸液には膠質液である plasgen（杏林）と同種新鮮血を用いた．

1. 輸液ならびに輸血後，肺動脈圧は中心静脈圧の3倍の上昇を示した．
2. 輸液の種類が晶質液，膠質液，血液の順に肺動脈圧は亢進した．
3. 輸液前に Isoproterenol Hydrochloride を投与しておくと肺動脈圧および中心静脈圧の上昇はある程度促進されたが，圧の下降は速かに行われた．
4. Phenoxybenzamine をあらかじめ投与すると輸液後の肺動脈圧亢進は著しく抑制された．

以上の成績から，大量輸液時の循環動態の判定には中心静脈圧のみでは不充分で肺動脈圧の測定が望ましい．大量輸液に伴う肺動脈圧亢進の防止には Isoproterenol よりも Phenoxybenzamine の方が効果的であることが明かにされた．